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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/506,978	02/18/2000	Francois Spertini	18519-001	9105

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MINTZ, LEVIN, COHN, FERRIS, GLOVSKY
AND POPEO, P.C.
ONE FINANCIAL CENTER
BOSTON, MA 02111

EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	

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23

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/506,978	Applicant(s) SPERTINI, FRANCOIS	
	Examiner " Neon" Phuong Huynh	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-30,36 and 44-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-30, 36, and 44-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/18/02 has been entered.

2. Claims 28-30, 36, and 44-49 are pending.

3. Claims 28-30, 36, and 44-49 are being acted upon in this Office Action.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 28-30, 36, and 44-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for a method of modulating an immune response, said method comprising administering a substantially pure polypeptide consisting of the amino acid sequence of SEQ ID NO: 1 to a subject in need thereof in an amount sufficient to inhibit an immune reaction by the subject against said polypeptide, the said method further comprising administering a second bee venom polypeptide selected from the group consisting of the ones recited in claim 30, **does not** reasonably provide enablement for (1) a method of modulating an immune response to bee venom, said method comprising administering a substantially pure bee venom polypeptide "**consisting essentially of**" the amino acid sequence of SEQ ID NO: 1 to a subject in need thereof in an amount sufficient to stimulate T-cell proliferation by the subject against said bee venom, (2) The method of modulating an immune response to bee venom, said method comprising administering a substantially pure bee venom polypeptide "**consisting essentially of**" the amino acid sequence of SEQ ID NO: 1 to a subject in need thereof in an amount sufficient to stimulate T-cell proliferation by the subject against said bee venom further comprising administering *any* "second bee venom polypeptide" to said subject, *any* second bee venom polypeptide is *any* "phospholipase A2 analogs or derivative thereof", *any* "hyaluronidase

analogs or derivatives thereof", *any* allergen C, *any* "allergen C analogs or derivatives thereof", *any* "mellitin analogs or derivatives thereof", *any* "minimine analogs or derivatives thereof", *any* protease inhibitor, *any* "protease inhibitor analogs or derivatives thereof", *any* "acid phosphatase analogs or derivatives thereof", *any* glycosylated IgE-binding proteins, *any* "glycosylated IgE-binding proteins analogs or derivatives thereof", (3) the said method further comprising administering one or more additional "bee venom polypeptides" to said subject, (4) a method of modulating an immune response to bee venom, said method comprising administering a composition comprising two overlapping bee venom polypeptide fragments, wherein said overlapping fragments form the entire amino acid sequence of SEQ ID NO: 1 to a subject in need thereof, in an amount sufficient to stimulate T-cell proliferation by the subject against said bee venom, wherein said overlapping fragments such as between "32 and 45 amino acids in length" (5) the said method further comprising administering one or more additional "bee venom polypeptides" to said subject, and (6) the said method wherein said two overlapping bee venom polypeptide fragments overlap by 3, 5 or 10 amino acids, and wherein said polypeptide fragments are between 32 and 40, or between 32 and 40 and between 32 and 45 amino acids in length, respectively for modulating any immune response. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only 4 full-length polypeptides of SEQ ID NOS: 1-4 for a method of **inhibiting** T cell response in a subject who is sensitive to a protein allergen from bee venom (see page 19). The specification discloses Api m 6 peptide of SEQ ID NO: 1 overlaps by at least 3, between 5 and 10 amino acids (See page 9 at lines 9-23 of specification). The specification further discloses fragments of SEQ ID NO: 1-4 wherein the fragment has Api m6

protein activities and can be, e.g., 6-72, 20-90, 30-70, or 40-60 amino acids in length on page 11 at lines 19-22.

The specification does not teach how to make and use *any* bee venom polypeptide "**consisting essentially of**" the amino acid sequence of SEQ ID NO: 1 as a method of modulating an immune response such as stimulate T cell proliferation because the term "consisting essentially of" is still open-ended. It expands the polypeptide of SEQ ID NO: 1 to include additional amino acids at either or both ends. Further, the specification does not define the term "consisting essentially of" and Applicant has not pointed out the support for said term. There is insufficient guidance as to the undisclosed amino acids to be added to SEQ ID NO: 1 and whether the resulting polypeptide after addition would maintain both structure and function, in turn, would be useful for modulating an immune response such as stimulating T cell proliferation.

There is no recognition in the art that sequence with identity predicts biological function. It is known in the art that even single amino acid changes or differences in a protein's amino acid sequence can have dramatic effects on the protein's function.

Attwood *et al* (of record) teach that "It is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences (and it is not always clear what we mean by "function"); very few structures are known compared with the number of sequences, and structure prediction methods are unreliable (and knowing structure does not inherently tell us functions)".

Fasler *et al.* (of record) teach that peptides derived from house dust mite Der p1 are modified by single amino acid substitutions at positions 173, 175, 176, 180 and 181 with alanine or glycine failed to induce Der p1 specific T cell proliferation and IL-2, IL-4 and IFN-γ production. Fasler *et al.* further teach that substituting a neutral Asn residue at position 173 either with a basic Lysine, a hydrophobic Try, Ile, an acidic Asp or a hydrophilic residue serine also did not induce T cell proliferation and cytokine production. However, substitution amino acid positions other than 173, 175, 176, 180 and 181 induces normal or only slightly reduced proliferative responses and cytokine production by T cells (page 524, in particular).

Burks *et al.* (of record) teach a modified allergen from peanut Ara h1 where the immunodominant IgE binding epitope of Ara h1 is modified by amino acid substitution at position 1, 3, 4 and 17 with alanine or glycine reduced IgE binding. In contrast, substituting an alanine for glutamine residue at position 31 leads to an increase IgE binding. Burks *et al.* further teach that "there is no obvious position within each peptide that when mutated, would result in

loss of IgE binding and there was no consensus in the type of amino acid that, when changed to alanine, would lead to loss of IgE binding" (See page 338, in particular).

Stanley *et al.* (of record) teach a modified peanut allergen Ara h2 by amino acid substitution with alanine at position 67, 68 or 69 significantly reduced IgE binding while substitution of serine residue at position 70 leads to an increased in IgE binding. Stanley et al also teach that in general, "each epitope could be mutated to a non-IgE binding peptide by the substitution of an alanine for a single amino acid residue. However, there was no obvious position within each peptide that, when mutated, would result in loss of IgE binding. Furthermore, there was no consensus in the type of amino acid that, when changed to alanine, would lead to loss of IgE binding" (See page 251, in particular).

Skolnick *et al* (of record) teach that sequence-based methods for function prediction are inadequate and knowing a protein's structure does not tell one its function (See abstract, in particular).

Colman *et al* (of record) teach that a single amino acid changes within the interface of antibody-antigen complex can abolish the antibody-antigen interaction or binding entirely (See page 33, in particular).

With regard to claim 29, the "second bee venom polypeptide" without SEQ ID NO has no structure, much less about the function, in turn, would be useful as a method of modulating any immune response. A polypeptide without the amino acid sequence has no structure. Given the indefinite number of undisclosed "second bee venom polypeptide", it is unpredictable which undisclosed "second bee venom polypeptide" would be useful for a method for modulating an immune response such as stimulating T cell proliferation. Further, there is insufficient working example demonstrating that any second bee venom polypeptide along with bee venom polypeptide consisting essentially of SEQ ID NO: 1 is effective for modulating an immune response. Given the indefinite number of undisclosed "second bee venom polypeptide", it would take undue amount of experimentation for one skill in the art to practice the claimed invention.

With regard to claims 30 and 46, the term "**analogs**", and "**derivatives thereof**" have no structure let alone having a specific function. There is insufficient guidance as how to make and much less how to use any analogs and derivatives such as the ones recited in claim 30 for a method of modulating any immune response because predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality requires a knowledge of and guidance with regard to which amino acids in the polypeptide's sequence, if

any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which a polypeptide's structure relates to its functional usefulness. It has been well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions can result in substantially different pharmacological activities.

Because of the lack of sufficient guidance and predictability in determining which modifications would lead to modulate any immune response such as stimulates T cell response and that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) was not well understood and was not predictable (e.g. see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.), it would require an undue amount of experimentation for one of skill in the art to arrive at the breadth of other functional analog and derivatives of phospholipase A2, hyaluronidase, allergen C, mellitin, adolapin, minimine, protease inhibitor, acid phosphatase, and glycosylated IgE-binding proteins for a method of modulating an immune response when administering along with bee venom polypeptide of SEQ ID NO: 1. Further, there is insufficient in vivo working example demonstrating any "analogs", "derivatives" are effective for the claimed method. With regard to "protease inhibitor", it is not clear which protease is the "protease" the inhibitor inhibits, let alone for a method of modulating any immune response. With regard to "glycosylated IgE-binding proteins", there is insufficient guidance as to the structure of "glycosylated-binding proteins" without SEQ ID NO, much less using it for the claimed method. Further, there is more than one "glycosylated-binding proteins". Given the indefinite number of undisclosed "analog", "derivatives", "protease inhibitor" and "glycosylated-binding proteins", it would take undue amount of experimentation even for one skill in the art to practice the claimed invention.

With regard to claims 36 and 45, it is not clear which additional "bee venom polypeptides" are intended for the claimed method. A protein is defined by its amino acid sequence and "Bee venom polypeptides" without SEQ ID NO again have no structure, let alone having a specific function. Without the amino acid sequence of any bee venom polypeptide, it would take undue amount of experimentation for one skill in the art to practice the claimed invention.

With regard to claims 44, and 47-49, the specification does not teach overlapping bee venom polypeptide fragments wherein the bee venom polypeptide fragments overlap by 3, **5 or**

10 amino acids and are between **32 and 38**, between **32 and 40** or between **32 and 45** amino acids in length. The specification discloses Api m 6 peptide of SEQ ID NO: 1 overlaps by at least 3, between 5 and 10 amino acids (See page 9 at lines 9-23 of specification). The specification further discloses fragments of SEQ ID NO: 1-4 wherein the fragment has Api m6 protein activities and can be, e.g., 6-72, 20-90, 30-70, or 40-60 amino acids in length on page 11 at lines 19-22. The specification does not describe nor enable any overlapping bee venom polypeptide fragments wherein the bee venom polypeptide fragments overlap by **5 or 10** amino acids and are between **32 and 38**, between **32 and 40** or between **32 and 45** amino acids in length other than those defined by SEQ ID NO. 1. This is new matter and required removal.

For these reasons, the specification as filed fails to enable one skill in the art to practice the invention as broadly as claimed without undue amount of experimentation. In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the lack of guidance and the lack of working examples, the breadth of the claims that fail to recite any structural or functional limitations and the unpredictability of the art, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicant's arguments filed 12/18/02 have been fully considered but are not found persuasive.

Applicant's position is that (1) the term "comprising" has been replace with the term "consisting essentially of" in claim 28 and the term "inhibit an immune reaction" with the phrase "stimulate T-cell proliferation". (2) The polypeptide fragment in claims 44 and 45-49 have been amended to require that the overlapping fragments form the entire sequence of SEQ ID NO: 1, and comprises between 32 and 45 amino acids. (3) It is routine for one of ordinary skill in the art to make 30 peptide fragments that overlap and when recite the entire amino acid sequence of SEQ ID NO: 1.

In response to Applicant's argument in item 1, the term "consisting essentially of" has no support in the specification as filed and it also changes the scope of the peptide. Further, the term "consisting essentially of" is still open-ended. It expands the polypeptide of SEQ ID NO: 1 to include additional amino acids at either or both ends.

In respond to Applicant's argument in items 2-3, the passages pointed out by applicant in the amendment filed 12/18/02 do not provide a clear support for the bee venom polypeptide fragments overlap by **5 or 10** amino acids and are between **32 and 38**, between **32 and 40** or

between **32 and 45** amino acids in length. This specific length as mentioned above and the specific overlapping fragment such as 5 or 10 amino acids are now NEW MATTER. The specification discloses Api m 6 peptide of SEQ ID NO: 1 overlaps by at least 3, between 5 and 10 amino acids (See page 9 at lines 9-23 of specification). The specification further discloses fragments of SEQ ID NO: 1-4 wherein the fragment has Api m6 protein activities and can be, e.g., 6-72, 20-90, 30-70, or 40-60 amino acids in length on page 11 at lines 19-22.

6. Claims 28-30, 36, and 44-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) a method of modulating an immune response to bee venom, said method comprising administering a substantially pure bee venom polypeptide "**consisting essentially of**" the amino acid sequence of SEQ ID NO: 1 to a subject in need thereof in an amount sufficient to stimulate T-cell proliferation by the subject against said bee venom, (2) The method of modulating an immune response to bee venom, said method comprising administering a substantially pure bee venom polypeptide "**consisting essentially of**" the amino acid sequence of SEQ ID NO: 1 to a subject in need thereof in an amount sufficient to stimulate T-cell proliferation by the subject against said bee venom further comprising administering *any* "second bee venom polypeptide" to said subject, *any* second bee venom polypeptide is *any* "phospholipase A2 analogs or derivative thereof", *any* "hyaluronidase analogs or derivatives thereof", *any* allergen C, *any* "allergen C analogs or derivatives thereof", *any* "mellitin analogs or derivatives thereof", *any* "minimine analogs or derivatives thereof", *any* protease inhibitor, *any* "protease inhibitor analogs or derivatives thereof", *any* "acid phosphatase analogs or derivatives thereof", *any* glycosylated IgE-binding proteins, *any* "glycosylated IgE-binding proteins analogs or derivatives thereof", (3) the said method further comprising administering one or more additional "bee venom polypeptides" to said subject, (4) a method of modulating an immune response to bee venom, said method comprising administering a composition comprising two overlapping bee venom polypeptide fragments, wherein said overlapping fragments form the entire amino acid sequence of SEQ ID NO: 1 to a subject in need thereof, in an amount sufficient to stimulate T-cell proliferation by the subject against said bee venom, wherein said overlapping fragments such as between "32 and 45

amino acids in length" (5) the said method further comprising administering one or more additional "bee venom polypeptides" to said subject, and (6) the said method wherein said two overlapping bee venom polypeptide fragments overlap by 3, 5 or 10 amino acids, and wherein said polypeptide fragments are between 32 and 40, or between 32 and 40 and between 32 and 45 amino acids in length, respectively for modulating any immune response.

The specification discloses only 4 full-length polypeptides of SEQ ID NOS: 1-4 for a method of inhibiting T cell response in a subject who is sensitive to a protein allergen from bee venom (see page 19). The specification discloses Api m 6 peptide of SEQ ID NO: 1 overlaps by at least 3, between 5 and 10 amino acids (See page 9 at lines 9-23 of specification). The specification further discloses fragments of SEQ ID NO: 1-4 wherein the fragment has Api m6 protein activities and can be, e.g., 6-72, 20-90, 30-70, or 40-60 amino acids in length on page 11 at lines 19-22.

With the exception of the specific bee venom polypeptide of SEQ ID NO: 1 mentioned above, there is insufficient written description about the structure associated with function of any bee venom polypeptide "consisting essentially of" because the term "consisting essentially of" is still open-ended. It expands the polypeptide of SEQ ID NO: 1 to include additional amino acids at either or both ends. The specification does not define said term. Further, there is also insufficient written description about any "second bee venom polypeptide", any "analogs", and any "derivatives" because said "second bee venom polypeptide", any "analogs", and any "derivatives" without SEQ ID NO has no structure, let alone having any function. Given the indefinite number of undisclosed "analog", "derivatives", "protease inhibitor" and "glycosylated-binding proteins", there is inadequate written description about the undisclosed "second bee venom polypeptide", "analogs", and "derivatives".

Further, there is insufficient written description about which protease is the "protease inhibitor" inhibits, much less for a method of modulating any immune response. Likewise, there is insufficient written description about "glycosylated IgE-binding proteins" because without SEQ ID NO, it has no structure, in turn, would be useful for the claimed method. Not only "glycosylated IgE-binding proteins" are not adequately described, there is more than one such undisclosed protein.

With regard to "stimulate T-cell proliferation", the specification on page 3 discloses that the method includes administering an Api m6 polypeptide of SEQ ID NO: 1 to a subject to

inhibit an immune reaction such as T-cell response or to diminish allergic response of a mammal (see page 19, at line 17) upon exposure to said polypeptide. Correction is required.

With regard to claims 44, and 47-49, there is insufficient written description about any overlapping bee venom polypeptide fragments wherein the bee venom polypeptide fragments overlap by 3, **5 or 10** amino acids and are between **32 and 38**, between **32 and 40** or between **32 and 45** amino acids in length, respectively. The specification discloses Api m 6 peptide of SEQ ID NO: 1 overlaps by at least 3, between 5 and 10 amino acids (See page 9 at lines 9-23 of specification). The specification further discloses fragments of SEQ ID NO: 1-4 wherein the fragment has Api m6 protein activities and can be, e.g., 6-72, 20-90, 30-70, or 40-60 amino acids in length on page 11 at lines 19-22. The specification does not describe any overlapping bee venom polypeptide fragments wherein the bee venom polypeptide fragments overlap by **5 or 10** amino acids and are between **32 and 38**, between **32 and 40** or between **32 and 45** amino acids in length other than those defined by SEQ ID NO. 1 for a method of modulating an immune response to stimulate T-cell proliferation. This is new matter.

Applicants' arguments filed 12/18/02 have been fully considered but are not found persuasive.

Applicant's position is that (1) claim 28 and dependent claims have been amended to recite a substantially pure bee venom polypeptide consisting essentially of SEQ ID NO: 1, as well as a specific way to modulating an immune reaction. (2) The polypeptide fragment in claims 44 and 45-49 have been amended to require that the overlapping fragments form the entire sequence of SEQ ID NO: 1, and comprises between 32 and 45 amino acids. (3) It is routine for one of ordinary skill in the art to make 30 peptide fragments that overlap and when recite the entire amino acid sequence of SEQ ID NO: 1.

In response to Applicant's argument in item 1, the term "consisting essentially of" has no support in the specification as filed and it also changes the scope of the peptide. Further, the term "consisting essentially of" is still open-ended. It expands the polypeptide of SEQ ID NO: 1 to include additional amino acids at either or both ends. Further, the specification on page 3 discloses that the method includes administering an Api m6 polypeptide of SEQ ID NO: 1 to a subject to **inhibit** an immune reaction such as T-cell response (see page 19, at line 17) upon exposure to said polypeptide.

In respond to Applicant's argument in items 2-3, the passages pointed out by applicant in the amendment filed 12/18/02 do not provide a clear support for the bee venom polypeptide

fragments overlap by **5 or 10** amino acids and are between **32 and 38**, between **32 and 40** or between **32 and 45** amino acids in length. This specific length as mentioned above and the specific overlapping fragment such as 5 or 10 amino acids are now NEW MATTER. The specification discloses Api m 6 peptide of SEQ ID NO: 1 overlaps by at least 3, between 5 and 10 amino acids (See page 9 at lines 9-23 of specification). The specification further discloses fragments of SEQ ID NO: 1-4 wherein the fragment has Api m6 protein activities and can be, e.g., 6-72, 20-90, 30-70, or 40-60 amino acids in length on page 11 at lines 19-22.

7. Claims 28-30, 36, and 44-49 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

The "consisting essentially of" in Claim 28 and dependent claims thereof represents a departure from the specification and the claims as originally filed. The passages pointed out by applicant in the amendment filed 12/18/02 do not provide a clear support for the said phrase.

The "between **32 and 45** amino acids in length" in claim 44 represents a departure from the specification and the claims as originally filed because the specification discloses only fragments of SEQ ID NO: 1-4 wherein the fragment has Api m6 protein activities and can be, e.g., 6-72, 20-90, 30-70, or 40-60 amino acids in length on page 11 at lines 19-22.

The "fragments are between 32 and 38 amino acids in length" in claim 47 represents a departure from the specification and the claims as originally filed because the specification discloses fragments of SEQ ID NO: 1-4 wherein the fragment has Api m6 protein activities and can be, e.g., 6-72, 20-90, 30-70, or 40-60 amino acids in length on page 11 at lines 19-22.

The "overlap by 5 amino acids" and "between 32 and 40 amino acids in length" in claim 48 represents a departure from the specification and the claims as originally filed. The specification discloses Api m 6 peptide of SEQ ID NO: 1 overlaps by at least 3, between 5 and 10 amino acids (See page 9 at lines 9-23 of specification). The specification further discloses fragments of SEQ ID NO: 1-4 wherein the fragment has Api m6 protein activities and can be, e.g., 6-72, 20-90, 30-70, or 40-60 amino acids in length on page 11 at lines 19-22.

The "overlap by 10 amino acids" and "between 32 and 45 amino acids in length" in claim 49 represents a departure from the specification and the claims as originally filed. The specification discloses Api m 6 peptide of SEQ ID NO: 1 overlaps by at least 3, between 5 and 10

amino acids (See page 9 at lines 9-23 of specification). The specification further discloses fragments of SEQ ID NO: 1-4 wherein the fragment has Api m6 protein activities and can be, e.g., 6-72, 20-90, 30-70, or 40-60 amino acids in length on page 11 at lines 19-22.

Applicants' arguments filed 12/18/02 have been fully considered but are not found persuasive.

The passages pointed out by applicant in the amendment filed 12/18/02 do not provide a clear support for the said phrases.

8. Claims 28-30, 36, and 44-49 are free of prior art.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

11. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
March 10, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600